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EXAMINER

SZPERKA, MICHAEL EDWARD

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

1. Applicant's after final submission received March 23, 2009 is acknowledged.

Claims 1-3, 5-8, 22-24, 26-29, 32-37, and 50-73 are pending.

No claims have been amended.

The declaration of inventor Dr. David B. Weiner is acknowledged and will be discussed in conjunction with applicant's arguments concerning the rejections of record.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-3, 5-7, 22-24, stand 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (WO 98/53843, of record) in view of Wang et al. (WO 99/67293, of record) in view of Hollis et al. (US 5,629,415, of record) and in view of Rutter (US Patent 4,769,326, of record) for the reasons of record.

The office action mailed January 23, 2009 states:

Chen et al. disclose vaccine constructs comprising the membrane bound domain of IgE coupled to heterologous sequences and excipients (see entire document, particularly the abstract and pages 3-5). These constructs are disclosed as being made recombinantly using vectors and host cells (see page 5). Note that heterologous antigens comprise helper T epitopes, and that

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Chen et al. disclose that their products are to be used in the suppression of IgE mediated responses, such as those that occur in allergy (see page 2).

The disclosure of Chen et al. differs from the instant claimed invention in that the nucleic acids of Chen et al. are not disclosed as being administered to a patient (i.e. the nucleic acids are not disclosed as a vaccine) nor are they disclosed as comprising a proteolytic cleavage sequence.

Wang et al. disclose vaccine constructs wherein IgE sequence is coupled to T helper epitopes such as those from tetanus toxoid, and wherein the administered construct is a nucleic acid (see entire document, particularly the abstract and pages 11, 13-14, 16, 20, 39-40). T helper epitopes from tetanus toxoid are preferred because they comprise the advantageous property of being promiscuous T helper epitopes that can be recognized by most members of a population expressing diverse MHC haplotypes (see particularly pages 16, 17, and 33). Wang et al. further disclose the desirability of inserting a linker sequence between IgE and T helper epitopes, such linkers offering the advantage of disrupting artificial secondary structures that result from directly joining the C-terminus of one epitope directly to the N-terminus of the other epitope and the advantage of acting as a flexible hinge that allows for more effective interactions with immune cells (see particularly page 32).

Hollis et al. disclose that recombinant IgE encoding polynucleotides can be inserted in to plasmid vectors and used to generate a wide variety of host cells including bacterial and mammalian cells (see entire document, particularly columns 4-7). Such host cells can be used to express polypeptides, with antibodies specific for the IgE constructs being used for affinity purification of the expressed polypeptide (see column 7).

Rutter discloses that the use of linkers comprising proteolytic cleavage sites is desirable in the manufacture of fusion constructs since said linkers allow for the efficient incorporation and removal of desired functional properties (see entire document, particularly the abstract). Such linkers allow for the separation the component parts of the fusion protein without otherwise causing degradation or proteolysis to the proteins or peptides of interest (see particularly columns 7, 8, 10, and 12).

Therefore, it would have been obvious to a person of ordinary skill at the time the instant invention was made to modify the nucleic acid constructs of Chen et al. to comprise promiscuous tetanus toxoid T helper epitopes so that they could be used in nucleic acid vaccines that would be effective in a majority of individuals in populations comprising diverse MHC haplotypes. Note that the use of nucleic acid vaccines was well known and routine in the art as disclosed by Wang et al. Such vaccines could be propagated in bacterial host cells as disclosed by Hollis et al. due to their ease of manufacture. A person of ordinary skill in the art would have been further motivated to incorporate proteolytic cleavage sequence linkers into such constructs since separation of epitopes provides the advantages of reduced unwanted secondary structure and increased flexibility as disclosed by Wang et al. and provides the advantage of allowing the component epitopes to be easily separated without excessive proteolytic degradation as disclosed by Rutter.

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that Chen et al. and Wang et al. teach away from the claimed invention because neither disclose the use of cleavable linker sequences and because Chen et al. disclose that there would be "no inhibition of IgE responses to unrelated, unconjugated antigens".

This argument is not persuasive. As stated in the rejection of record, an ordinary artisan would have been motivated to add a cleavage sequence between the

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components of a fusion protein as an aid in the construction of said fusion protein since they allow for the efficient incorporation and removal of functional properties as disclosed by Rutter et al. Applicant has assumed that the fusion protein encoded by the claimed polynucleotide will separate into two separate molecules upon expression in vivo. However, this assumption is not a limitation recited in the present claims. Further, many of the enzymes contemplated for use by Rutter et al., such as Aspergillopeptidase B, are not proteins expressed in IgE-producing animals (see for example columns 15-16 of Rutter et al.). Thus, the possibility that components of the fusion protein can be separated does not mean that they will be separated. Further, applicant has claimed the polynucleotide sequence, not the polypeptide, and the uses and motivations to make these distinct products need not be the same.

Applicant further argues Wang et al. similarly disclose a desire for additional antigenic epitopes to adjacent either N- or C- terminal to IgE peptide sequences and thus also teach away from a construct which can be reduced into its constituent components.

This argument is not persuasive for the reasons discussed above in reference to the teachings of Chen et al.

The rejection is maintained.

4. Claims 1-3, 5-7, 22-24, and 26-29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/20038 (of record) in view of Wang et al. (WO 99/67293, of record) and in view of Rutter (US Patent 4,769,326, of record) for the reasons of record.

The office action mailed January 23, 2009 states:

The '038 document discloses nucleic acid molecules comprising the membrane anchoring region of B-cell bound IgE linked to a foreign T helper epitope (see entire document, particularly the abstract and pages 37 and 41). Helper T epitopes are disclosed as coming from tetanus toxoid (see particularly page 30). These nucleic acids are further disclosed as being present in plasmids and viral vectors for use in vaccines comprising excipients (see particularly pages 52-56 and 66-67). The nucleic acids of the '038 document are also disclosed as being present in bacterial and mammalian cells for use in production of recombinant polypeptides (see particularly pages 60-66). These teachings differ from the claimed invention in that they do not disclose the use of linkers comprising a proteolytic cleavage sequence between the epitopes.

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Wang et al. disclose vaccine constructs wherein IgE sequence is coupled to T helper epitopes such as those from tetanus toxoid, and wherein the administered construct is a nucleic acid (see entire document, particularly the abstract and pages 11, 13-14, 16, 20, 39-40). T helper epitopes from tetanus toxoid are preferred because they comprise the advantageous property of being promiscuous T helper epitopes that can be recognized by most members of a population expressing diverse MHC haplotypes (see particularly pages 16, 17, and 33). Wang et al. further disclose the desirability of inserting a linker sequence between IgE and T helper epitopes, such linkers offering the advantage of disrupting artificial secondary structures that result from directly joining the C-terminus of one epitope directly to the N-terminus of the other epitope and the advantage of acting as a flexible hinge that allows for more effective interactions with immune cells (see particularly page 32).

Rutter discloses that the use of linkers comprising proteolytic cleavage sites is desirable in the manufacture of fusion constructs since said linkers allow for the efficient incorporation and removal of desired functional properties (see entire document, particularly the abstract). Such linkers allow for the separation the component parts of the fusion protein without otherwise causing degradation or proteolysis to the proteins or peptides of interest (see particularly columns 7, 8, 10, and 12).

Therefore, it would have been obvious to a person of ordinary skill at the time the instant invention was made to modify the nucleic acid constructs of the '038 document to comprise proteolytic cleavage sequence linkers since separation of epitopes provides the advantages of reduced unwanted secondary structure and increased flexibility as disclosed by Wang et al. and provides the advantage of allowing the component epitopes to be easily separated without excessive proteolytic degradation as disclosed by Rutter.

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. As discussed above, applicant argues that Wang et al. teaches away from the claimed invention.

This argument is not persuasive for the reasons discussed supra.

5. Claims 1-3, 5-7, 22-24, and 26-29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Klysner et al. (US2002/0172673, of record) in view of Wang et al. (WO 99/67293, of record) and in view of Rutter (US Patent 4,769,326, of record) for the reasons of record.

The office action mailed January 23, 2009 states:

Klysner et al. disclose nucleic acid molecules comprising the membrane anchoring region of B-cell bound IgE linked to a foreign T helper epitope (see entire document, particularly the abstract and paragraphs 121 and 132). Helper T epitopes are disclosed as coming from tetanus toxoid (see particularly paragraph 101). These nucleic acids are further disclosed as being present in plasmids and viral vectors for use in vaccines comprising excipients (see particularly paragraphs 171- 180 and 214-219). The nucleic acids of Klysner et al. are also disclosed as being present in bacterial and mammalian cells for use in production of recombinant polypeptides (see particularly paragraphs 198-213). This disclosure differs from the claimed invention in that Klysner et al. do not disclose the use of linkers comprising a proteolytic cleavage sequence between the epitopes.

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Wang et al. disclose vaccine constructs wherein IgE sequence is coupled to T helper epitopes such as those from tetanus toxoid, and wherein the administered construct is a nucleic acid (see entire document, particularly the abstract and pages 11, 13-14, 16, 20, 39-40). T helper epitopes from tetanus toxoid are preferred because they comprise the advantageous property of being promiscuous T helper epitopes that can be recognized by most members of a population expressing diverse MHC haplotypes (see particularly pages 16, 17, and 33). Wang et al. further disclose the desirability of inserting a linker sequence between IgE and T helper epitopes, such linkers offering the advantage of disrupting artificial secondary structures that result from directly joining the C-terminus of one epitope directly to the N-terminus of the other epitope and the advantage of acting as a flexible hinge that allows for more effective interactions with immune cells (see particularly page 32).

Rutter discloses that the use of linkers comprising proteolytic cleavage sites is desirable in the manufacture of fusion constructs since said linkers allow for the efficient incorporation and removal of desired functional properties (see entire document, particularly the abstract). Such linkers allow for the separation the component parts of the fusion protein without otherwise causing degradation or proteolysis to the proteins or peptides of interest (see particularly columns 7, 8, 10, and 12).

Therefore, it would have been obvious to a person of ordinary skill at the time the instant invention was made to modify the nucleic acid constructs of Klysner et al. to comprise proteolytic cleavage sequence linkers since separation of epitopes provides the advantages of reduced unwanted secondary structure and increased flexibility as disclosed by Wang et al. and provides the advantage of allowing the component epitopes to be easily separated without excessive proteolytic degradation as disclosed by Rutter.

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that Klysner et al. (in addition to Wang et al. which has been addressed supra) teaches away from using cleavable linkers because if the fusion proteins of Klysner et al. are separated into component polypeptides, the efficiency of antigen presentation will be diminished.

This argument is not persuasive because as was discussed above in conjunction with the teachings of Chen et al. the claims do not recite that the encoded fusion protein ever is cleaved in vivo or that the proteolytic cleavage sequence present in the polypeptides encoded by the claimed polynucleotides are recognized by an enzyme present in the bloodstream of an IgE bearing animal. See also the discussion of Chen et al. that appears supra. Thus applicant is arguing limitations not claimed, and therefore the rejection is maintained.

6. Claims 8, 32-37, 50, and 58-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (WO 98/53843, of record) in view of Wang et al. (WO 99/67293, of record) in view of Hollis et al. (US 5,629,415, of record) and in view of

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Rutter (US Patent 4,769,326, of record) as applied to claims 1-3, 5-7, 22-24, and 26-29 above, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929, see entire document) as evidenced by Janeway et al. (Immunobiology, 3rd edition, Garland Publications, 1997, pages 3:26-3:31) for the reasons of record.

The office action mailed January 23, 2009 states:

The inventions rendered obvious by the disclosures of Chen et al., Wang et al. Hollis et al., and Rutter have been discussed above and differ from the claimed invention in that while they disclose the recombinant production of secreted polypeptides, they do not specify that the leader sequence used in such constructs is "an IgE leader sequence".

Walls et al. disclose vectors for the expression immunoglobulin polypeptides (see entire document, particularly the abstract). These vectors comprise the immunoglobulin (Ig) leader sequence. The Ig leader of Walls et al. comprises an intron which must be spliced out prior to translation (see particularly Figure 1, the last full paragraph on page 2924, and the paragraph spanning the left and right columns of page 2925). It is known that introns are essential for the efficient expression of Ig genes and that the presence of intronic sequences in expression vectors enhances expression of the inserted gene of interest (see particularly the bottom right column of page 2924).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make recombinant constructs, vectors and host cells comprising the Ig leader sequence disclosed by Walls et al. Motivation to do so at the time the invention was made comes from the teachings of Walls et al. that the Ig leader sequence encodes an intron and that the presence of introns is essential for efficient expression of Ig constructs, such as chimeric IgE polypeptides. Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such, the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain (FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and thus an "IgE leader" is the same sequence as an IgM, IgD, IgG, and IgA leader sequence since the constant domain exons are not expressed without being joined to an already rearranged variable domain. Thus the "Ig leader" of Walls et al. is an "IgE leader".

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that the leader sequence used in the instant invention is distinct from the prior art of Walls et al. and has submitted the declaration of inventor Weiner to support this position.

Neither applicant's arguments nor the declaration are persuasive. The declaration provides an alignment of sequences which are purported to be the leader sequences of immunoglobulins. The source of these sequences, such as GenBank accession numbers, or what organism(s) they are from are not provided. Further, some of the sequences are described as being "IgA constant" and "IgG constant". The constant domain is not expressed as a separate polypeptide in vivo and is always joined

to the variable domain of immunoglobulin assembled via the process of V(D)J recombination. As such it is unclear how or why inventor Weiner has chosen the labels attached to the sequences of the alignment.

As shown in figures 3.26 and 3.28 of Janeway et al., the leader sequence is upstream of the variable domain and this same assembly can be joined to multiple distinct constant domains via the process of isotype/class switching. It is well known in the art that hybridomas expressing a monoclonal antibody can undergo class switching upon exposure to exogenous agents, such as IL-4 (Muller et al., Jabara et al., and Chu et al.). This allows researchers to construct families of antibodies whose members differ from each other only in their heavy chain isotype (see particularly the left column of page 877 of Muller et al.). The variable domain and its attached leader sequence do not change even though the heavy chain isotype is changed. As such, there cannot be a leader that is an "IgE" leader since any given rearranged immunoglobulin locus (which initially is expressed with an IgM isotype) has the potential to class switch to IgE and secrete IgE rather than IgM.

As shown by Watson et al., there are approximately 250 different heavy chain locus V genes which can participate the process of V(D)J recombination (page 866 and table 23-3). Each V gene has its own leader sequence, as is made explicitly clear in figure 23-26 of Watson et al. Thus, there are potentially 250 distinct leader sequences that may be present in a rearranged immunoglobulin gene. Thus, finding that the leader of a sequence deposited in a database as an IgE antibody is different from the leader from another sequence deposited as an IgG1 antibody is only reflective of the diversity of leader sequences present in the heavy chain V genes and has no bearing on constant domain isotype since the same V(D)J rearranged sequence can be present with any heavy chain constant domain due to isotype switching (see figure 23.36 of Watson et al.). Neither applicant's arguments nor inventor Weiner's declaration address this basic aspect of B cell biology. Note that Muller et al., Jabara et al., Chu et al. and Watson et al. are presented solely to rebut the argument and declaration that "IgE leaders" are somehow distinct from other immunoglobulin leaders and to demonstrate basic B cell biology that would be well known to ordinary artisans in the field of

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immunology. They are not part of the rejection of record nor are they needed for the rejection of record to be logically and scientifically complete.

7. Claims 8, 32-37, 50, and 58-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/20038 (of record) in view of Wang et al. (WO 99/67293, of record) and in view of Rutter (US Patent 4,769,326, of record) as applied to claims 1-3, 5-7, 22-24, and 26-29 above, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929, see entire document) as evidenced by Janeway et al. (Immunobiology, 3rd edition, Garland Publications, 1997, pages 3:26-3:31) for the reasons of record.

The office action mailed January 23, 2009 states:

The inventions rendered obvious by the disclosures of the '038 document, Wang et al., and Rutter have been discussed above and differ from the claimed invention in that while they disclose the recombinant production of secreted polypeptides, they do not specify that the leader sequence used in such constructs is "an IgE leader sequence".

Walls et al. disclose vectors for the expression immunoglobulin polypeptides (see entire document, particularly the abstract). These vectors comprise the immunoglobulin (Ig) leader sequence. The Ig leader of Walls et al. comprises an intron which must be spliced out prior to translation (see particularly Figure 1, the last full paragraph on page 2924, and the paragraph spanning the left and right columns of page 2925). It is known that introns are essential for the efficient expression of Ig genes and that the presence of intronic sequences in expression vectors enhances expression of the inserted gene of interest (see particularly the bottom right column of page 2924).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make recombinant constructs, vectors and host cells comprising the Ig leader sequence disclosed by Walls et al. Motivation to do so at the time the invention was made comes from the teachings of Walls et al. that the Ig leader sequence encodes an intron and that the presence of introns is essential for efficient expression of Ig constructs, such as chimeric IgE polypeptides. Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such, the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain (FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and thus an "IgE leader" is the same sequence as an IgM, IgD, IgG, and IgA leader sequence since the constant domain exons are not expressed without being joined to an already rearranged variable domain. Thus the "Ig leader" of Walls et al. is an "IgE leader".

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that "IgE" leaders are structurally distinct.

This argument is not persuasive for the reasons discussed above. The rejection is maintained.

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8. Claims 8, 32-37, 50, and 58-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Klysner et al. (US2002/0172673, of record) in view of Wang et al. (WO 99/67293, of record) and in view of Rutter (US Patent 4,769,326) as applied to claims 1-3, 5-7, 22-24, and 26-29 above, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929, see entire document) as evidenced by Janeway et al. (Immunobiology, 3rd edition, Garland Publications, 1997, pages 3:26-3:31) for the reasons of record.

The office action mailed January 23, 2009 states:

The inventions rendered obvious by the disclosures of Klysner et al., Wang et al., and Rutter have been discussed above and differ from the claimed invention in that while they disclose the recombinant production of secreted polypeptides, they do not specify that the leader sequence used in such constructs is "an IgE leader sequence".

Walls et al. disclose vectors for the expression immunoglobulin polypeptides (see entire document, particularly the abstract). These vectors comprise the immunoglobulin (Ig) leader sequence. The Ig leader of Walls et al. comprises an intron which must be spliced out prior to translation (see particularly Figure 1, the last full paragraph on page 2924, and the paragraph spanning the left and right columns of page 2925). It is known that introns are essential for the efficient expression of Ig genes and that the presence of intronic sequences in expression vectors enhances expression of the inserted gene of interest (see particularly the bottom right column of page 2924).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make recombinant constructs, vectors and host cells comprising the Ig leader sequence disclosed by Walls et al. Motivation to do so at the time the invention was made comes from the teachings of Walls et al. that the Ig leader sequence encodes an intron and that the presence of introns is essential for efficient expression of Ig constructs, such as chimeric IgE polypeptides. Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such, the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain (FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and thus an "IgE leader" is the same sequence as an IgM, IgD, IgG, and IgA leader sequence since the constant domain exons are not expressed without being joined to an already rearranged variable domain. Thus the "Ig leader" of Walls et al. is an "IgE leader".

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that "IgE" leaders are structurally distinct.

This argument is not persuasive for the reasons discussed above. The rejection is maintained.

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9. Claims 8, 32-37, 50, and 66-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Klysner et al. (US2002/0172673) in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929, see entire document) as evidenced by Janeway et al. (Immunobiology, 3rd edition, Garland Publications, 1997, pages 3:26-3:31) for the reasons of record.

The office action mailed January 23, 2009 states:

Klysner et al. disclose nucleic acid molecules comprising the membrane anchoring region of B-cell bound IgE linked to a foreign T helper epitope (see entire document, particularly the abstract and paragraphs 121 and 132). Helper T epitopes are disclosed as coming from tetanus toxoid (see particularly paragraph 101). These nucleic acids are further disclosed as being present in plasmids and viral vectors for use in vaccines comprising excipients (see particularly paragraphs 171- 180 and 214-219). The nucleic acids of Klysner et al. are also disclosed as being present in bacterial and mammalian cells for use in production of recombinant polypeptides (see particularly paragraphs 198-213). This disclosure differs from the instant claimed invention in that it is not specified that the leader sequence sued for the expression of soluble polypeptides is and "IgE leader".

Walls et al. disclose vectors for the expression immunoglobulin polypeptides (see entire document, particularly the abstract). These vectors comprise the immunoglobulin (Ig) leader sequence. The Ig leader of Walls et al. comprises an intron which must be spliced out prior to translation (see particularly Figure 1, the last full paragraph on page 2924, and the paragraph spanning the left and right columns of page 2925). It is known that introns are essential for the efficient expression of Ig genes and that the presence of intronic sequences in expression vectors enhances expression of the inserted gene of interest (see particularly the bottom right column of page 2924).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make recombinant constructs, vectors and host cells comprising the Ig leader sequence disclosed by Walls et al. Motivation to do so at the time the invention was made comes from the teachings of Walls et al. that the Ig leader sequence encodes an intron and that the presence of introns is essential for efficient expression of Ig constructs, such as chimeric IgE polypeptides of Klysner et al. Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such, the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain (FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and thus an "IgE leader" is the same sequence as an IgM, IgD, IgG, and IgA leader sequence since the constant domain exons are not expressed without being joined to an already rearranged variable domain. Thus the "Ig leader" of Walls et al. is an "IgE leader".

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that "IgE" leaders are structurally distinct.

This argument is not persuasive for the reasons discussed above. The rejection is maintained.

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10. Claims 8, 32-37, 50, and 66-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/20038 (of record) in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929, see entire document) as evidenced by Janeway et al. (Immunobiology, 3rd edition, Garland Publications, 1997, pages 3:26-3:31) for the reasons of record.

The office action mailed January 23, 2009 states:

The '038 document discloses nucleic acid molecules comprising the membrane anchoring region of B-cell bound IgE linked to a foreign T helper epitope (see entire document, particularly the abstract and pages 37 and 41). Helper T epitopes are disclosed as coming from tetanus toxoid (see particularly page 30). These nucleic acids are further disclosed as being present in plasmids and viral vectors for use in vaccines comprising excipients (see particularly pages 52-56 and 66-67). The nucleic acids of the '038 document are also disclosed as being present in bacterial and mammalian cells for use in production of recombinant polypeptides (see particularly pages 60-66). This disclosure differs from the instant claimed invention in that it is not specified that the leader sequence used for the expression of soluble polypeptides is an "IgE leader".

Walls et al. disclose vectors for the expression immunoglobulin polypeptides (see entire document, particularly the abstract). These vectors comprise the immunoglobulin (Ig) leader sequence. The Ig leader of Walls et al. comprises an intron which must be spliced out prior to translation (see particularly Figure 1, the last full paragraph on page 2924, and the paragraph spanning the left and right columns of page 2925). It is known that introns are essential for the efficient expression of Ig genes and that the presence of intronic sequences in expression vectors enhances expression of the inserted gene of interest (see particularly the bottom right column of page 2924).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make recombinant constructs, vectors and host cells comprising the Ig leader sequence disclosed by Walls et al. Motivation to do so at the time the invention was made comes from the teachings of Walls et al. that the Ig leader sequence encodes an intron and that the presence of introns is essential for efficient expression of Ig constructs, such as chimeric IgE polypeptides of the '038 document. Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such, the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain (FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and thus an "IgE leader" is the same sequence as an IgM, IgD, IgG, and IgA leader sequence since the constant domain exons are not expressed without being joined to an already rearranged variable domain. Thus the "Ig leader" of Walls et al. is an "IgE leader".

Applicant's arguments filed March 23, 2009 have been fully considered but they are not persuasive. Applicant argues that "IgE" leaders are structurally distinct.

This argument is not persuasive for the reasons discussed above. The rejection is maintained.

11. No claims are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Primary Examiner
Art Unit 1644

/Michael Szperka/
Primary Examiner, Art Unit 1644